SEQUENCE LISTING

<110> Sharma, Satish Kumar
      Rank, Kenneth Bruce

<120> SOLUBLE NOTCH-BASED SUBSTRATES FOR GAMMA SECRETASE AND METHODS AND
COMPOSITIONS FOR USING SAME

<130> PC27514A

<140> 10/717,244

<141> 2003-11-19

<160> 14

<170> PatentIn version 3.1

<210> 1
<211> 2190
<212> DNA
<213> Artificial sequence

<220>
<223> DNA encoding synthetic fusion of notch and nus

<400> 1

```
atgaacaaag aaattttggc tgtagttgaa gccgtatcca atgaaaaggc gctacctcgc      60

gagaagattt tcgaagcatt ggaaagcgcg ctggcgacag caacaaagaa aaaatatgaa     120

caagagatcg acgtccgcgt acagatcgat cgcaaaagcg gtgattttga cactttccgt     180

cgctggttag ttgttgatga agtcacccag ccgaccaagg aaatcaccct tgaagccgca     240

cgttatgaag atgaaagcct gaacctgggc gattacgttg aagatcagat tgagtctgtt     300

acctttgacc gtatcactac ccagacggca aaacaggtta tcgtgcagaa agtgcgtgaa     360

gccgaacgtg cgatggtggt tgatcagttc cgtgaacacg aaggtgaaat catcaccggc     420

gtggtgaaaa aagtaaaccg cgacaacatc tctctggatc tgggcaacaa cgctgaagcc     480

gtgatcctgc gcgaagatat gctgccgcgt gaaaacttcc gccctggcga ccgcgttcgt     540

ggcgtgctct attccgttcg cccggaagcg cgtggcgcgc aactgttcgt cactcgttcc     600

aagccggaaa tgctgatcga actgttccgt attgaagtgc agaaatcgg cgaagaagtg      660

attgaaatta aagcagcggc tcgcgatccg ggttctcgtg cgaaaatcgc ggtgaaaacc     720

aacgataaac gtatcgatcc ggtaggtgct tgcgtaggta tgcgtggcgc gcgtgttcag     780

gcggtgtcta ctgaactggg tggcgagcgt atcgatatcg tcctgtggga tgataacccg     840

gcgcagttcg tgattaacgc aatggcaccg gcagacgttg cttctatcgt ggtggatgaa     900

gataaacaca ccatggacat cgccgttgaa gccggtaatc tggcgcaggc gattggccgt     960

aacggtcaga acgtgcgtct ggcttcgcaa ctgagcggtt gggaactcaa cgtgatgacc    1020

gttgacgacc tgcaagctaa gcatcaggcg gaagcgcacg cagcgatcga caccttcacc    1080
```

```
aaatatctcg acatcgacga agacttcgcg actgttctgg tagaagaagg cttctcgacg      1140

ctggaagaat tggcctatgt gccgatgaaa gagctgttgg aaatcgaagg ccttgatgag      1200

ccgaccgttg aagcactgcg cgagcgtgct aaaaatgcac tggccaccat tgcacaggcc      1260

caggaagaaa gcctcggtga taacaaaccg gctgacgatc tgctgaacct tgaagggggta     1320

gatcgtgatt tggcattcaa actggccgcc cgtggcgttt gtacgctgga agatctcgcc      1380

gaacagggca ttgatgatct ggctgatatc gaagggttga ccgacgaaaa agccggagca      1440

ctgattatgg ctgcccgtaa tatttgctgg ttcggtgacg aagcgactag tggttctggt      1500

catcaccatc accatcactc cgcgggtaaa gaaaccgctg ctgcgaaatt tgaacgccag      1560

cacatggact cgccaccgcc aactggtctg gtcccccggg gcagcgcggg ttctggtacg      1620

attgatgacg acgacaagag tccgggagct cgtggatccg aattcaatat tccttacaag      1680

attgaggccg tgaagagtga gccggtggag cctccgctgc cctcgcagct gcacctcatg      1740

tacgtggcag cggccgcctt cgtgctcctg ttctttgtgg gctgtggggt gctgctgtcc      1800

cgcaagcgcc ggcggcagca tggccagctc tggttccctg agggtttcaa agtgtcagag      1860

gccagcaaga agaagcggag agagcccctc ggcgaggact cagtcggcct caagcccctg      1920

aagaatgcct cagatggtgc tctgatggac gacaatcaga acgagtgggg agacgaagac      1980

ctggagacca agaagttccg gtttgaggag ccagtagttc tccctgacct gagtgatcag      2040

actgaccaca gacagtggac ccagcagcac ctggacgctg ctgacctgcg catgtctgcc      2100

atggcccccaa caccgcctca gggggaggtg gatgctgacg attataaaga cgatgacgat      2160

aaacaccatc accatcacca tcaccattga                                       2190
```

<210> 2
<211> 729
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic fusion protein sequence of notch and nus

<400> 2

Met Asn Lys Glu Ile Leu Ala Val Val Glu Ala Val Ser Asn Glu Lys
1   5   10   15

Ala Leu Pro Arg Glu Lys Ile Phe Glu Ala Leu Glu Ser Ala Leu Ala
                20   25   30

Thr Ala Thr Lys Lys Lys Tyr Glu Gln Glu Ile Asp Val Arg Val Gln
            35   40   45

Ile Asp Arg Lys Ser Gly Asp Phe Asp Thr Phe Arg Arg Trp Leu Val
        50   55   60

```
Val Asp Glu Val Thr Gln Pro Thr Lys Glu Ile Thr Leu Glu Ala Ala
65                  70              75                      80

Arg Tyr Glu Asp Glu Ser Leu Asn Leu Gly Asp Tyr Val Glu Asp Gln
                85              90                      95

Ile Glu Ser Val Thr Phe Asp Arg Ile Thr Thr Gln Thr Ala Lys Gln
            100             105                 110

Val Ile Val Gln Lys Val Arg Glu Ala Glu Arg Ala Met Val Val Asp
        115             120                 125

Gln Phe Arg Glu His Glu Gly Glu Ile Ile Thr Gly Val Val Lys Lys
    130             135                 140

Val Asn Arg Asp Asn Ile Ser Leu Asp Leu Gly Asn Asn Ala Glu Ala
145             150             155                     160

Val Ile Leu Arg Glu Asp Met Leu Pro Arg Glu Asn Phe Arg Pro Gly
            165             170                 175

Asp Arg Val Arg Gly Val Leu Tyr Ser Val Arg Pro Glu Ala Arg Gly
        180             185                 190

Ala Gln Leu Phe Val Thr Arg Ser Lys Pro Glu Met Leu Ile Glu Leu
    195             200                 205

Phe Arg Ile Glu Val Pro Glu Ile Gly Glu Glu Val Ile Glu Ile Lys
    210             215                 220

Ala Ala Ala Arg Asp Pro Gly Ser Arg Ala Lys Ile Ala Val Lys Thr
225             230             235                     240

Asn Asp Lys Arg Ile Asp Pro Val Gly Ala Cys Val Gly Met Arg Gly
            245             250                 255

Ala Arg Val Gln Ala Val Ser Thr Glu Leu Gly Gly Glu Arg Ile Asp
        260             265                 270

Ile Val Leu Trp Asp Asp Asn Pro Ala Gln Phe Val Ile Asn Ala Met
    275             280                 285

Ala Pro Ala Asp Val Ala Ser Ile Val Val Asp Glu Asp Lys His Thr
    290             295                 300

Met Asp Ile Ala Val Glu Ala Gly Asn Leu Ala Gln Ala Ile Gly Arg
305             310             315                     320

Asn Gly Gln Asn Val Arg Leu Ala Ser Gln Leu Ser Gly Trp Glu Leu
```

325   330   335

Asn Val Met Thr Val Asp Asp Leu Gln Ala Lys His Gln Ala Glu Ala
            340   345   350

His Ala Ala Ile Asp Thr Phe Thr Lys Tyr Leu Asp Ile Asp Glu Asp
        355   360   365

Phe Ala Thr Val Leu Val Glu Glu Gly Phe Ser Thr Leu Glu Glu Leu
    370   375   380

Ala Tyr Val Pro Met Lys Glu Leu Leu Glu Ile Glu Gly Leu Asp Glu
385   390   395   400

Pro Thr Val Glu Ala Leu Arg Glu Arg Ala Lys Asn Ala Leu Ala Thr
                405   410   415

Ile Ala Gln Ala Gln Glu Glu Ser Leu Gly Asp Asn Lys Pro Ala Asp
            420   425   430

Asp Leu Leu Asn Leu Glu Gly Val Asp Arg Asp Leu Ala Phe Lys Leu
        435   440   445

Ala Ala Arg Gly Val Cys Thr Leu Glu Asp Leu Ala Glu Gln Gly Ile
    450   455   460

Asp Asp Leu Ala Asp Ile Glu Gly Leu Thr Asp Glu Lys Ala Gly Ala
465   470   475   480

Leu Ile Met Ala Ala Arg Asn Ile Cys Trp Phe Gly Asp Glu Ala Thr
                485   490   495

Ser Gly Ser Gly His His His His His Ser Ala Gly Lys Glu Thr
            500   505   510

Ala Ala Ala Lys Phe Glu Arg Gln His Met Asp Ser Pro Pro Thr
        515   520   525

Gly Leu Val Pro Arg Gly Ser Ala Gly Ser Gly Thr Ile Asp Asp Asp
    530   535   540

Asp Lys Ser Pro Gly Ala Arg Gly Ser Glu Phe Asn Ile Pro Tyr Lys
545   550   555   560

Ile Glu Ala Val Lys Ser Glu Pro Val Glu Pro Pro Leu Pro Ser Gln
                565   570   575

Leu His Leu Met Tyr Val Ala Ala Ala Ala Phe Val Leu Leu Phe Phe
            580   585   590

Val Gly Cys Gly Val Leu Leu Ser Arg Lys Arg Arg Arg Gln His Gly
        595   600   605

Gln Leu Trp Phe Pro Glu Gly Phe Lys Val Ser Glu Ala Ser Lys Lys
    610   615   620

Lys Arg Arg Glu Pro Leu Gly Glu Asp Ser Val Gly Leu Lys Pro Leu
625   630   635   640

Lys Asn Ala Ser Asp Gly Ala Leu Met Asp Asp Asn Gln Asn Glu Trp
            645   650   655

Gly Asp Glu Asp Leu Glu Thr Lys Lys Phe Arg Phe Glu Glu Pro Val
            660   665   670

Val Leu Pro Asp Leu Ser Asp Gln Thr Asp His Arg Gln Trp Thr Gln
        675   680   685

Gln His Leu Asp Ala Ala Asp Leu Arg Met Ser Ala Met Ala Pro Thr
    690   695   700

Pro Pro Gln Gly Glu Val Asp Ala Asp Asp Tyr Lys Asp Asp Asp Asp
705   710   715   720

Lys His His His His His His His His
                725

<210>   3
<211>   525
<212>   DNA
<213>   Artificial sequence

<220>
<223>   Wildtype notch DNA sequence

<400>   3

aatattcctt acaagattga ggccgtgaag agtgagccgg tggagcctcc gctgccctcg   60
cagctgcacc tcatgtacgt ggcagcggcc gccttcgtgc tcctgttctt tgtgggctgt   120
ggggtgctgc tgtcccgcaa gcgccggcgg cagcatggcc agctctggtt ccctgagggt   180
ttcaaagtgt cagaggccag caagaagaag cggagagagc ccctcggcga ggactcagtc   240
ggcctcaagc ccctgaagaa tgcctcagat ggtgctctga tggacgacaa tcagaacgag   300
tggggagacg aagacctgga gaccaagaag ttccggtttg aggagccagt agttctccct   360
gacctgagtg atcagactga ccacagacag tggacccagc agcacctgga cgctgctgac   420
ctgcgcatgt ctgccatggc cccaacaccg cctcaggggg aggtggatgc tgacgattat   480
aaagacgatg acgataaaca ccatcaccat caccatcacc attga   525

<210> 4
<211> 174
<212> PRT
<213> Artificial sequence

<220>
<223> Wildtype notch protein sequence

<400> 4

```
Asn Ile Pro Tyr Lys Ile Glu Ala Val Lys Ser Glu Pro Val Glu Pro
1               5                   10                  15

Pro Leu Pro Ser Gln Leu His Leu Met Tyr Val Ala Ala Ala Ala Phe
            20                  25                  30

Val Leu Leu Phe Phe Val Gly Cys Gly Val Leu Leu Ser Arg Lys Arg
            35                  40                  45

Arg Arg Gln His Gly Gln Leu Trp Phe Pro Glu Gly Phe Lys Val Ser
    50                  55                  60

Glu Ala Ser Lys Lys Lys Arg Arg Glu Pro Leu Gly Glu Asp Ser Val
65                  70                  75                  80

Gly Leu Lys Pro Leu Lys Asn Ala Ser Asp Gly Ala Leu Met Asp Asp
            85                  90                  95

Asn Gln Asn Glu Trp Gly Asp Glu Asp Leu Glu Thr Lys Lys Phe Arg
            100                 105                 110

Phe Glu Glu Pro Val Val Leu Pro Asp Leu Ser Asp Gln Thr Asp His
        115                 120                 125

Arg Gln Trp Thr Gln Gln His Leu Asp Ala Ala Asp Leu Arg Met Ser
    130                 135                 140

Ala Met Ala Pro Thr Pro Pro Gln Gly Glu Val Asp Ala Asp Asp Tyr
145                 150                 155                 160

Lys Asp Asp Asp Asp Lys His His His His His His His
                165                 170
```

<210> 5
<211> 2531
<212> PRT
<213> Mus musculus

<400> 5

```
Met Pro Arg Leu Leu Thr Pro Leu Leu Cys Leu Thr Leu Leu Pro Ala
1               5                   10                  15
```

Arg Ala Ala Arg Gly Leu Arg Cys Ser Gln Pro Ser Gly Thr Cys Leu
            20   25   30

Asn Gly Gly Arg Cys Glu Val Ala Ser Gly Thr Glu Ala Cys Val Ala
        35   40   45

Ser Gly Ser Phe Val Gly Gln Arg Cys Gln Asp Pro Asn Pro Cys Leu
    50   55   60

Ser Thr Arg Cys Lys Asn Ala Gly Thr Cys Tyr Val Val Asp His Gly
65   70   75   80

Gly Ile Val Asp Tyr Ala Cys Ser Cys Pro Leu Gly Phe Ser Gly Pro
            85   90   95

Leu Cys Leu Thr Pro Leu Asp Lys Pro Cys Leu Ala Asn Pro Cys Arg
            100   105   110

Asn Gly Gly Thr Cys Asp Leu Leu Thr Leu Thr Glu Tyr Lys Cys Arg
        115   120   125

Cys Ser Pro Gly Trp Ser Gly Lys Ser Cys Gln Gln Ala Asp Pro Cys
    130   135   140

Ala Ser Asn Pro Cys Ala Asn Gly Gly Gln Cys Leu Pro Phe Glu Ser
145   150   155   160

Ser Tyr Ile Cys Arg Cys Pro Pro Gly Phe His Gly Pro Thr Cys Arg
            165   170   175

Gln Asp Val Asn Glu Cys Ser Gln Asn Pro Gly Leu Cys Arg His Gly
        180   185   190

Gly His Cys His Asn Glu Ile Gly Ser Tyr Arg Cys Ala Cys Cys Ala
        195   200   205

Thr His Thr Gly Pro His Cys Glu Leu Pro Tyr Val Pro Cys Ser Pro
    210   215   220

Ser Pro Cys Gln Asn Gly Ala Thr Cys Arg Pro Thr Gly Asp Thr Thr
225   230   235   240

His Glu Cys Ala Cys Leu Pro Gly Phe Ala Gly Gln Asn Cys Glu Glu
            245   250   255

Asn Val Asp Asp Cys Pro Gly Asn Asn Cys Lys Asn Gly Gly Ala Cys
            260   265   270

```
Val Asp Gly Val Asn Thr Tyr Asn Cys Arg Cys Pro Pro Glu Val Thr
        275             280             285

Gly Gln Tyr Cys Thr Glu Asp Val Asp Glu Cys Gln Leu Met Pro Asn
    290             295             300

Ala Cys Gln Asn Ala Gly Thr Cys His Asn Thr His Gly Gly Tyr Asn
305             310             315             320

Cys Val Cys Val Asn Gly Trp Thr Gly Glu Asp Cys Ser Glu Asn Ile
            325             330             335

Asp Asp Cys Ala Ser Ala Ala Cys Phe Gln Gly Ala Thr Cys His Asp
        340             345             350

Arg Val Ala Ser Phe Tyr Cys Glu Cys Pro His Gly Arg Thr Gly Leu
    355             360             365

Leu Cys His Leu Lys His Ala Cys Ile Ser Asn Pro Cys Asn Glu Gly
    370             375             380

Ser Asn Cys Asp Thr Asn Pro Val Asn Gly Lys Arg Ile Cys Thr Cys
385             390             395             400

Pro Ser Gly Tyr Thr Gly Pro Ala Cys Ser Gln Asp Val Asp Glu Cys
            405             410             415

Asp Leu Gly Ala Asn Arg Cys Glu His Ala Gly Lys Cys Leu Asn Thr
            420             425             430

Leu Gly Ser Phe Glu Cys Gln Cys Leu Gln Gly Tyr Thr Gly Pro Gly
    435             440             445

Cys Glu Ile Asp Val Asn Glu Cys Ile Ser Asn Pro Cys Gln Asn Asp
    450             455             460

Ala Thr Cys Leu Asp Gln Ile Gly Glu Phe Gln Cys Ile Cys Met Pro
465             470             475             480

Gly Tyr Glu Gly Val Tyr Cys Glu Ile Asn Thr Asp Glu Cys Ala Ser
            485             490             495

Ser Pro Cys Leu His Asn Gly His Cys Met Asp Lys Ile His Glu Phe
        500             505             510

Gln Cys Gln Cys Pro Lys Gly Phe Asn Gly His Leu Cys Gln Tyr Asp
    515             520             525
```

```
Val Asp Glu Cys Ala Ser Thr Pro Cys Lys Asn Gly Ala Lys Cys Leu
    530                     535                 540

Asp Gly Pro Asn Thr Tyr Thr Cys Val Cys Thr Glu Gly Tyr Thr Gly
545                 550                 555                 560

Thr His Cys Glu Val Asp Ile Asp Glu Cys Asp Pro Asp Pro Cys His
                565             570                 575

Tyr Gly Ser Cys Lys Asp Gly Val Ala Thr Phe Thr Cys Leu Cys Gln
            580                 585             590

Pro Gly Tyr Thr Gly His His Cys Glu Thr Asn Ile Asn Glu Cys His
        595             600                 605

Ser Gln Pro Cys Arg His Gly Gly Thr Cys Gln Asp Arg Asp Asn Ser
    610             615                 620

Tyr Leu Cys Leu Cys Leu Lys Gly Thr Thr Gly Pro Asn Cys Glu Ile
625                 630                 635                 640

Asn Leu Asp Asp Cys Ala Ser Asn Pro Cys Asp Ser Gly Thr Cys Leu
            645             650                 655

Asp Lys Ile Asp Gly Tyr Glu Cys Ala Cys Glu Pro Gly Tyr Thr Gly
            660             665             670

Ser Met Cys Asn Val Asn Ile Asp Glu Cys Ala Gly Ser Pro Cys His
        675             680                 685

Asn Gly Gly Thr Cys Glu Asp Gly Ile Ala Gly Phe Thr Cys Arg Cys
    690             695                 700

Pro Glu Gly Tyr His Asp Pro Thr Cys Leu Ser Glu Val Asn Glu Cys
705             710             715                 720

Asn Ser Asn Pro Cys Ile His Gly Ala Cys Arg Asp Gly Leu Asn Gly
            725             730                 735

Tyr Lys Cys Asp Cys Ala Pro Gly Trp Ser Gly Thr Asn Cys Asp Ile
            740             745                 750

Asn Asn Asn Glu Cys Glu Ser Asn Pro Cys Val Asn Gly Gly Thr Cys
        755             760                 765

Lys Asp Met Thr Ser Gly Tyr Val Cys Thr Cys Arg Glu Gly Phe Ser
    770             775                 780

Gly Pro Asn Cys Gln Thr Asn Ile Asn Glu Cys Ala Ser Asn Pro Cys
```

```
        785                    790                    795                    800

Leu Asn Gln Gly Thr Cys Ile Asp Asp Val Ala Gly Tyr Lys Cys Asn
                 805             810                     815

Cys Pro Leu Pro Tyr Thr Gly Ala Thr Cys Glu Val Val Leu Ala Pro
                 820             825                 830

Cys Ala Thr Ser Pro Cys Lys Asn Ser Gly Val Cys Lys Glu Ser Glu
             835                 840                 845

Asp Tyr Glu Ser Phe Ser Cys Val Cys Pro Thr Gly Trp Gln Gly Gln
        850                 855                 860

Thr Cys Glu Val Asp Ile Asn Glu Cys Val Lys Ser Pro Cys Arg His
865                 870                     875                 880

Gly Ala Ser Cys Gln Asn Thr Asn Gly Ser Tyr Arg Cys Leu Cys Gln
                 885                 890                     895

Ala Gly Tyr Thr Gly Arg Asn Cys Glu Ser Asp Ile Asp Asp Cys Arg
             900                 905                 910

Pro Asn Pro Cys His Asn Gly Gly Ser Cys Thr Asp Gly Ile Asn Thr
         915                 920                 925

Ala Phe Cys Asp Cys Leu Pro Gly Phe Gln Gly Ala Phe Cys Glu Glu
    930             935                 940

Asp Ile Asn Glu Cys Ala Ser Asn Pro Cys Gln Asn Gly Ala Asn Cys
945             950             955                     960

Thr Asp Cys Val Asp Ser Tyr Thr Cys Thr Cys Pro Val Gly Phe Asn
                 965             970                 975

Gly Ile His Cys Glu Asn Asn Thr Pro Asp Cys Thr Glu Ser Ser Cys
             980             985                 990

Phe Asn Gly Gly Thr Cys Val Asp Gly Ile Asn Ser Phe Thr Cys Leu
         995             1000                1005

Cys Pro Pro Gly Phe Thr Gly Ser Tyr Cys Gln Tyr Asp Val Asn
    1010            1015               1020

Glu Cys Asp Ser Arg Pro Cys Leu His Gly Gly Thr Cys Gln Asp
    1025            1030               1035

Ser Tyr Gly Thr Tyr Lys Cys Thr Cys Pro Gln Gly Tyr Thr Gly
    1040            1045               1050
```

```
Leu Asn  Cys Gln Asn Leu Val  Arg Trp Cys Asp Ser  Ala Pro Cys
    1055             1060             1065

Lys Asn  Gly Gly Arg Cys Trp  Gln Thr Asn Thr Gln  Tyr His Cys
    1070             1075             1080

Glu Cys  Arg Ser Gly Trp Thr  Gly Val Asn Cys Asp  Val Leu Ser
    1085             1090             1095

Val Ser  Cys Glu Val Ala Ala  Gln Lys Arg Gly Ile  Asp Val Thr
    1100             1105             1110

Leu Leu  Cys Gln His Gly Gly  Leu Cys Val Asp Glu  Gly Asp Lys
    1115             1120             1125

His Tyr  Cys His Cys Gln Ala  Gly Tyr Thr Gly Ser  Tyr Cys Glu
    1130             1135             1140

Asp Glu  Val Asp Glu Cys Ser  Pro Asn Pro Cys Gln  Asn Gly Ala
    1145             1150             1155

Thr Cys  Thr Asp Tyr Leu Gly  Gly Phe Ser Cys Lys  Cys Val Ala
    1160             1165             1170

Gly Tyr  His Gly Ser Asn Cys  Ser Glu Glu Ile Asn  Glu Cys Leu
    1175             1180             1185

Ser Gln  Pro Cys Gln Asn Gly  Gly Thr Cys Ile Asp  Leu Thr Asn
    1190             1195             1200

Ser Tyr  Lys Cys Ser Cys Pro  Arg Gly Thr Gln Gly  Val His Cys
    1205             1210             1215

Glu Ile  Asn Val Asp Asp Cys  His Pro Pro Leu Asp  Pro Ala Ser
    1220             1225             1230

Arg Ser  Pro Lys Cys Phe Asn  Asn Gly Thr Cys Val  Asp Gln Val
    1235             1240             1245

Gly Gly  Tyr Thr Cys Thr Cys  Pro Pro Gly Phe Val  Gly Glu Arg
    1250             1255             1260

Cys Glu  Gly Asp Val Asn Glu  Cys Leu Ser Asn Pro  Cys Asp Pro
    1265             1270             1275

Arg Gly  Thr Gln Asn Cys Val  Gln Arg Val Asn Asp  Phe His Cys
    1280             1285             1290
```

```
Glu Cys  Arg Ala Gly His Thr  Gly Arg Arg Cys Glu  Ser Val Ile
    1295                 1300                 1305

Asn Gly  Cys Arg Gly Lys Pro  Cys Lys Asn Gly Gly  Val Cys Ala
    1310                 1315                 1320

Val Ala  Ser Asn Thr Ala Arg  Gly Phe Ile Cys Arg  Cys Pro Ala
    1325                 1330                 1335

Gly Phe  Glu Gly Ala Thr Cys  Glu Asn Asp Ala Arg  Thr Cys Gly
    1340                 1345                 1350

Ser Leu  Arg Cys Leu Asn Gly  Gly Thr Cys Ile Ser  Gly Pro Arg
    1355                 1360                 1365

Ser Pro  Thr Cys Leu Cys Leu  Gly Ser Phe Thr Gly  Pro Glu Cys
    1370                 1375                 1380

Gln Phe  Pro Ala Ser Ser Pro  Cys Val Gly Ser Asn  Pro Cys Tyr
    1385                 1390                 1395

Asn Gln  Gly Thr Cys Glu Pro  Thr Ser Glu Asn Pro  Phe Tyr Arg
    1400                 1405                 1410

Cys Leu  Cys Pro Ala Lys Phe  Asn Gly Leu Leu Cys  His Ile Leu
    1415                 1420                 1425

Asp Tyr  Ser Phe Thr Gly Gly  Ala Gly Pro Asp Ile  Pro Pro Pro
    1430                 1435                 1440

Gln Ile  Glu Glu Ala Cys Glu  Leu Pro Glu Cys Gln  Val Asp Ala
    1445                 1450                 1455

Gly Asn  Lys Val Cys Asn Leu  Gln Cys Asn Asn His  Ala Cys Gly
    1460                 1465                 1470

Trp Asp  Gly Gly Asp Cys Ser  Leu Asn Phe Asn Asp  Pro Trp Lys
    1475                 1480                 1485

Asn Cys  Thr Gln Ser Leu Gln  Cys Trp Lys Tyr Phe  Ser Asp Gly
    1490                 1495                 1500

His Cys  Asp Ser Gln Cys Asn  Ser Ala Gly Cys Leu  Phe Asp Gly
    1505                 1510                 1515

Phe Asp  Cys Gln Leu Thr Glu  Gly Gln Cys Asn Pro  Leu Tyr Asp
    1520                 1525                 1530
```

```
Gln Tyr  Cys Lys Asp His Phe  Ser Asp Gly His Cys  Asp Gln Gly
    1535                 1540              1545

Cys Asn  Ser Ala Glu Cys Glu  Trp Asp Gly Leu Asp  Cys Ala Glu
    1550                 1555              1560

His Val  Pro Glu Arg Leu Ala  Ala Gly Thr Leu Val  Leu Val Val
    1565                 1570              1575

Leu Leu  Pro Pro Asp Gln Leu  Arg Asn Asn Ser Phe  His Phe Leu
    1580                 1585              1590

Arg Glu  Leu Ser His Val Leu  His Thr Asn Val Val  Phe Lys Arg
    1595                 1600              1605

Asp Ala  Gln Gly Gln Gln Met  Ile Phe Pro Tyr Tyr  Gly His Glu
    1610                 1615              1620

Glu Glu  Leu Arg Lys His Pro  Ile Lys Arg Ser Thr  Val Gly Trp
    1625                 1630              1635

Ala Thr  Ser Ser Leu Leu Pro  Gly Thr Ser Gly Gly  Arg Gln Arg
    1640                 1645              1650

Arg Glu  Leu Asp Pro Met Asp  Ile Arg Gly Ser Ile  Val Tyr Leu
    1655                 1660              1665

Glu Ile  Asp Asn Arg Gln Cys  Val Gln Ser Ser Ser  Gln Cys Phe
    1670                 1675              1680

Gln Ser  Ala Thr Asp Val Ala  Ala Phe Leu Gly Ala  Leu Ala Ser
    1685                 1690              1695

Leu Gly  Ser Leu Asn Ile Pro  Tyr Lys Ile Glu Ala  Val Lys Ser
    1700                 1705              1710

Glu Pro  Val Glu Pro Pro Leu  Pro Ser Gln Leu His  Leu Met Tyr
    1715                 1720              1725

Val Ala  Ala Ala Ala Phe Val  Leu Leu Phe Phe Val  Gly Cys Gly
    1730                 1735              1740

Val Leu  Leu Ser Arg Lys Arg  Arg Arg Gln His Gly  Gln Leu Trp
    1745                 1750              1755

Phe Pro  Glu Gly Phe Lys Val  Ser Glu Ala Ser Lys  Lys Lys Arg
    1760                 1765              1770

Arg Glu  Pro Leu Gly Glu Asp  Ser Val Gly Leu Lys  Pro Leu Lys
```

```
        1775                      1780                      1785

Asn Ala  Ser Asp Gly Ala Leu  Met Asp Asp Asn Gln  Asn Glu Trp
    1790                  1795                  1800

Gly Asp  Glu Asp Leu Glu Thr  Lys Lys Phe Arg Phe  Glu Glu Pro
    1805                  1810                  1815

Val Val  Leu Pro Asp Leu Ser  Asp Gln Thr Asp His  Arg Gln Trp
    1820                  1825                  1830

Thr Gln  Gln His Leu Asp Ala  Ala Asp Leu Arg Met  Ser Ala Met
    1835                  1840                  1845

Ala Pro  Thr Pro Pro Gln Gly  Glu Val Asp Ala Asp  Cys Met Asp
    1850                  1855                  1860

Val Asn  Val Arg Gly Pro Asp  Gly Phe Thr Pro Leu  Met Ile Ala
    1865                  1870                  1875

Ser Cys  Ser Gly Gly Gly Leu  Glu Thr Gly Asn Ser  Glu Glu Glu
    1880                  1885                  1890

Glu Asp  Ala Pro Ala Val Ile  Ser Asp Phe Ile Tyr  Gln Gly Ala
    1895                  1900                  1905

Ser Leu  His Asn Gln Thr Asp  Arg Thr Gly Glu Thr  Ala Leu His
    1910                  1915                  1920

Leu Ala  Ala Arg Tyr Ser Arg  Ser Asp Arg Arg Lys  Arg Leu Glu
    1925                  1930                  1935

Ala Ser  Ala Asp Ala Asn Ile  Gln Asp Asn Met Gly  Arg Thr Pro
    1940                  1945                  1950

Leu His  Ala Ala Val Ser Ala  Asp Ala Gln Gly Val  Phe Gln Ile
    1955                  1960                  1965

Leu Leu  Arg Asn Arg Ala Thr  Asp Leu Asp Ala Arg  Met His Asp
    1970                  1975                  1980

Gly Thr  Thr Pro Leu Ile Leu  Ala Ala Arg Leu Ala  Val Glu Gly
    1985                  1990                  1995

Met Leu  Glu Asp Leu Ile Asn  Ser His Ala Asp Val  Asn Ala Val
    2000                  2005                  2010

Asp Asp  Leu Gly Lys Ser Ala  Leu His Trp Ala Ala  Ala Val Asn
    2015                  2020                  2025
```

```
Asn Val  Asp Ala Ala Val Val  Leu Leu Lys Asn Gly  Ala Asn Lys
    2030             2035              2040

Asp Ile  Glu Asn Asn Lys Glu  Glu Thr Ser Leu Phe  Leu Ser Ile
    2045             2050              2055

Arg Arg  Glu Ser Tyr Glu Thr  Ala Lys Val Leu Leu  Asp His Phe
    2060             2065              2070

Ala Asn  Arg Asp Ile Thr Asp  His Met Asp Arg Leu  Pro Arg Asp
    2075             2080              2085

Ile Ala  Gln Glu Arg Met His  His Asp Ile Val Arg  Leu Leu Asp
    2090             2095              2100

Glu Tyr  Asn Leu Val Arg Ser  Pro Gln Leu His Gly  Thr Ala Leu
    2105             2110              2115

Gly Gly  Thr Pro Thr Leu Ser  Pro Thr Leu Cys Ser  Pro Asn Gly
    2120             2125              2130

Tyr Pro  Gly Asn Leu Lys Ser  Ala Thr Gln Gly Lys  Lys Ala Arg
    2135             2140              2145

Lys Pro  Ser Thr Lys Gly Leu  Ala Cys Gly Ser Lys  Glu Ala Lys
    2150             2155              2160

Asp Leu  Lys Ala Arg Arg Lys  Ser Ser Gln Asp Gly  Lys Gly Trp
    2165             2170              2175

Leu Leu  Asp Ser Ser Ser Ser  Met Leu Ser Pro Val  Asp Ser Leu
    2180             2185              2190

Glu Ser  Pro His Gly Tyr Leu  Ser Asp Val Ala Ser  His Pro Leu
    2195             2200              2205

Leu Pro  Ser Pro Phe Gln Gln  Ser Pro Ser Met Pro  Leu Ser His
    2210             2215              2220

Leu Pro  Gly Met Pro Asp Thr  His Leu Gly Ile Ser  His Leu Asn
    2225             2230              2235

Val Ala  Ala Lys Pro Glu Met  Ala Ala Leu Ala Gly  Gly Ser Arg
    2240             2245              2250

Leu Ala  Phe Glu His Pro Pro  Pro Arg Leu Ser His  Leu Pro Val
    2255             2260              2265
```

Ala Ser Ser Ala Cys Thr Val Leu Ser Thr Asn Gly Thr Gly Ala
    2270   2275   2280

Met Asn Phe Thr Val Gly Ala Pro Ala Ser Leu Asn Gly Gln Cys
    2285   2290   2295

Glu Trp Leu Pro Arg Leu Gln Asn Gly Met Val Pro Ser Gln Tyr
    2300   2305   2310

Asn Pro Leu Arg Pro Gly Val Thr Pro Gly Thr Leu Ser Thr Gln
    2315   2320   2325

Ala Ala Gly Leu Gln His Ser Met Met Gly Pro Leu His Ser Ser
    2330   2335   2340

Leu Ser Thr Asn Thr Leu Ser Pro Ile Ile Tyr Gln Gly Leu Pro
    2345   2350   2355

Asn Thr Arg Leu Ala Thr Gln Pro His Leu Val Gln Thr Gln Gln
    2360   2365   2370

Val Gln Pro Gln Asn Leu Pro Leu Gln Pro Gln Asn Leu Gln Pro
    2375   2380   2385

Pro Ser Gln Pro His Leu Ser Val Ser Ser Ala Ala Asn Gly His
    2390   2395   2400

Leu Gly Arg Ser Phe Leu Ser Gly Glu Pro Ser Gln Ala Asp Val
    2405   2410   2415

Gln Pro Leu Gly Pro Ser Ser Leu Pro Val His Thr Ile Leu Pro
    2420   2425   2430

Gln Glu Ser Gln Ala Leu Pro Thr Ser Leu Pro Ser Ser Met Val
    2435   2440   2445

Pro Pro Met Thr Thr Thr Gln Phe Leu Thr Pro Pro Ser Gln His
    2450   2455   2460

Ser Tyr Ser Ser Ser Pro Val Asp Asn Thr Pro Ser His Gln Leu
    2465   2470   2475

Gln Val Pro Glu Pro Thr Phe Leu Thr Pro Ser Pro Glu Ser Pro
    2480   2485   2490

Asp Gln Trp Ser Ser Ser Ser Pro His Ser Asn Ile Ser Asp Trp
    2495   2500   2505

```
Ser Glu  Gly Ile Ser Ser Pro  Pro Thr Thr Met Pro  Ser Gln Ile
    2510               2515              2520


Thr His  Ile Pro Glu Ala Phe  Lys
    2525               2530
```

<210> 6
<211> 2444
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<222> (891)..(891)
<223> Xaa = Any or unknown amino acid

<220>
<221> misc_feature
<222> (1763)..(1763)
<223> Xaa = Any or unknown amino acid

<220>
<221> misc_feature
<222> (1787)..(1787)
<223> Xaa = Any or unknown amino acid

<400> 6

```
Met Pro Pro Leu Leu Ala Pro Leu Leu Cys Leu Ala Leu Leu Pro Ala
1               5               10              15


Leu Ala Ala Arg Gly Pro Arg Cys Ser Gln Pro Gly Glu Thr Cys Leu
            20              25              30


Asn Gly Gly Lys Cys Glu Ala Ala Asn Gly Thr Glu Ala Cys Val Cys
        35              40              45


Gly Gly Ala Phe Val Gly Pro Arg Cys Gln Asp Pro Asn Pro Cys Leu
    50              55              60


Ser Thr Pro Cys Lys Asn Ala Gly Thr Cys His Val Val Asp Arg Arg
65              70              75              80


Gly Val Ala Asp Tyr Ala Cys Ser Cys Ala Leu Gly Phe Ser Gly Pro
            85              90              95


Leu Cys Leu Thr Pro Leu Asp Asn Ala Cys Leu Thr Asn Pro Cys Arg
            100             105             110


Asn Gly Gly Thr Cys Asp Leu Leu Thr Leu Thr Glu Tyr Lys Cys Arg
        115             120             125


Cys Pro Pro Gly Trp Ser Gly Lys Ser Cys Gln Gln Ala Asp Pro Cys
```

```
        130                    135                    140

Ala Ser Asn Pro Cys Ala Asn Gly Gly Gln Cys Leu Pro Phe Glu Ala
145                 150                 155                 160

Ser Tyr Ile Cys His Cys Pro Pro Ser Phe His Gly Pro Thr Cys Arg
                165                 170                 175

Gln Asp Val Asn Glu Cys Gly Gln Lys Pro Arg Leu Cys Arg His Gly
            180                 185                 190

Gly Thr Cys His Asn Glu Val Gly Ser Tyr Arg Cys Val Cys Arg Ala
        195                 200                 205

Thr His Thr Gly Pro Asn Cys Glu Arg Pro Tyr Val Pro Cys Ser Pro
    210                 215                 220

Ser Pro Cys Gln Asn Gly Gly Thr Cys Arg Pro Thr Gly Asp Val Thr
225                 230                 235                 240

His Glu Cys Ala Cys Leu Pro Gly Phe Thr Gly Gln Asn Cys Glu Glu
            245                 250                 255

Asn Ile Asp Asp Cys Pro Gly Asn Asn Cys Lys Asn Gly Gly Ala Cys
            260                 265                 270

Val Asp Gly Val Asn Thr Tyr Asn Cys Pro Cys Pro Pro Glu Trp Thr
        275                 280                 285

Gly Gln Tyr Cys Thr Glu Asp Val Asp Glu Cys Gln Leu Met Pro Asn
    290                 295                 300

Ala Cys Gln Asn Gly Gly Thr Cys His Asn Thr His Gly Gly Tyr Asn
305                 310                 315                 320

Cys Val Cys Val Asn Gly Trp Thr Gly Glu Asp Cys Ser Glu Asn Ile
            325                 330                 335

Asp Asp Cys Ala Ser Ala Ala Cys Phe His Gly Ala Thr Cys His Asp
            340                 345                 350

Arg Val Ala Ser Phe Tyr Cys Glu Cys Pro His Gly Arg Thr Gly Leu
        355                 360                 365

Leu Cys His Leu Asn Asp Ala Cys Ile Ser Asn Pro Cys Asn Glu Gly
    370                 375                 380

Ser Asn Cys Asp Thr Asn Pro Val Asn Gly Lys Ala Ile Cys Thr Cys
385                 390                 395                 400
```

```
Pro Ser Gly Tyr Thr Gly Pro Ala Cys Ser Gln Asp Val Asp Glu Cys
            405         410              415

Ser Leu Gly Ala Asn Pro Cys Glu His Ala Gly Lys Cys Ile Asn Thr
            420         425              430

Leu Gly Ser Phe Glu Cys Gln Cys Leu Gln Gly Tyr Thr Gly Pro Arg
            435         440              445

Cys Glu Ile Asp Val Asn Glu Cys Val Ser Asn Pro Cys Gln Asn Asp
    450             455         460

Ala Thr Cys Leu Asp Gln Ile Gly Glu Phe Gln Cys Met Cys Met Pro
465             470             475              480

Gly Tyr Glu Gly Val His Cys Glu Val Asn Thr Asp Glu Cys Ala Ser
            485             490              495

Ser Pro Cys Leu His Asn Gly Arg Cys Leu Asp Lys Ile Asn Glu Phe
            500             505              510

Gln Cys Glu Cys Pro Thr Gly Phe Thr Gly His Leu Cys Gln Tyr Asp
        515             520              525

Val Asp Glu Cys Ala Ser Thr Pro Cys Lys Asn Gly Ala Lys Cys Leu
    530             535              540

Asp Gly Pro Asn Thr Tyr Thr Cys Val Cys Thr Glu Gly Tyr Thr Gly
545             550             555              560

Thr His Cys Glu Val Asp Ile Asp Glu Cys Asp Pro Asp Pro Cys His
            565             570              575

Tyr Gly Ser Cys Lys Asp Gly Val Ala Thr Phe Thr Cys Leu Cys Arg
            580             585              590

Pro Gly Tyr Thr Gly His His Cys Glu Thr Asn Ile Asn Glu Cys Ser
            595             600              605

Ser Gln Pro Cys Arg Leu Arg Gly Thr Cys Gln Asp Pro Asp Asn Ala
    610             615              620

Tyr Leu Cys Phe Cys Leu Lys Gly Thr Thr Gly Pro Asn Cys Glu Ile
625             630             635              640

Asn Leu Asp Asp Cys Ala Ser Ser Pro Cys Asp Ser Gly Thr Cys Leu
            645             650              655
```

Asp Lys Ile Asp Gly Tyr Glu Cys Ala Cys Glu Pro Gly Tyr Thr Gly
        660   665   670

Ser Met Cys Asn Ser Asn Ile Asp Glu Cys Ala Gly Asn Pro Cys His
        675   680   685

Asn Gly Gly Thr Cys Glu Asp Gly Ile Asn Gly Phe Thr Cys Arg Cys
    690   695   700

Pro Glu Gly Tyr His Asp Pro Thr Cys Leu Ser Glu Val Asn Glu Cys
705   710   715   720

Asn Ser Asn Pro Cys Val His Gly Ala Cys Arg Asp Ser Leu Asn Gly
            725   730   735

Tyr Lys Cys Asp Cys Asp Pro Gly Trp Ser Gly Thr Asn Cys Asp Ile
        740   745   750

Asn Asn Asn Glu Cys Glu Ser Asn Pro Cys Val Asn Gly Gly Thr Cys
        755   760   765

Lys Asp Met Thr Ser Gly Ile Val Cys Thr Cys Arg Glu Gly Phe Ser
    770   775   780

Gly Pro Asn Cys Gln Thr Asn Ile Asn Glu Cys Ala Ser Asn Pro Cys
785   790   795   800

Leu Asn Lys Gly Thr Cys Ile Asp Asp Val Ala Gly Tyr Lys Cys Asn
            805   810   815

Cys Leu Leu Pro Tyr Thr Gly Ala Thr Cys Glu Val Val Leu Ala Pro
        820   825   830

Cys Ala Pro Ser Pro Cys Arg Asn Gly Gly Glu Cys Arg Gln Ser Glu
        835   840   845

Asp Tyr Glu Ser Phe Ser Cys Val Cys Pro Thr Ala Gly Ala Lys Gly
    850   855   860

Gln Thr Cys Glu Val Asp Ile Asn Glu Cys Val Leu Ser Pro Cys Arg
865   870   875   880

His Gly Ala Ser Cys Gln Asn Thr His Gly Xaa Tyr Arg Cys His Cys
            885   890   895

Gln Ala Gly Tyr Ser Gly Arg Asn Cys Glu Thr Asp Ile Asp Asp Cys
        900   905   910

Arg Pro Asn Pro Cys His Asn Gly Gly Ser Cys Thr Asp Gly Ile Asn
    915   920   925

Thr Ala Phe Cys Asp Cys Leu Pro Gly Phe Arg Gly Thr Phe Cys Glu
    930   935   940

Glu Asp Ile Asn Glu Cys Ala Ser Asp Pro Cys Arg Asn Gly Ala Asn
945   950   955   960

Cys Thr Asp Cys Val Asp Ser Tyr Thr Cys Thr Cys Pro Ala Gly Phe
            965   970   975

Ser Gly Ile His Cys Glu Asn Asn Thr Pro Asp Cys Thr Glu Ser Ser
            980   985   990

Cys Phe Asn Gly Gly Thr Cys Val Asp Gly Ile Asn Ser Phe Thr Cys
        995   1000   1005

Leu Cys Pro Pro Gly Phe Thr Gly Ser Tyr Cys Gln His Val Val
    1010   1015   1020

Asn Glu Cys Asp Ser Arg Pro Cys Leu Leu Gly Gly Thr Cys Gln
    1025   1030   1035

Asp Gly Arg Gly Leu His Arg Cys Thr Cys Pro Gln Gly Tyr Thr
    1040   1045   1050

Gly Pro Asn Cys Gln Asn Leu Val His Trp Cys Asp Ser Ser Pro
    1055   1060   1065

Cys Lys Asn Gly Gly Lys Cys Trp Gln Thr His Thr Gln Tyr Arg
    1070   1075   1080

Cys Glu Cys Pro Ser Gly Trp Thr Gly Leu Tyr Cys Asp Val Pro
    1085   1090   1095

Ser Val Ser Cys Glu Val Ala Ala Gln Arg Gln Gly Val Asp Val
    1100   1105   1110

Ala Arg Leu Cys Gln His Gly Gly Leu Cys Val Asp Ala Gly Asn
    1115   1120   1125

Thr His His Cys Arg Cys Gln Ala Gly Tyr Thr Gly Ser Tyr Cys
    1130   1135   1140

Glu Asp Leu Val Asp Glu Cys Ser Pro Ser Pro Cys Gln Asn Gly
    1145   1150   1155

Ala Thr Cys Thr Asp Tyr Leu Gly Gly Tyr Ser Cys Lys Cys Val

Ala Gly Tyr His Gly Val Asn Cys Ser Glu Glu Ile Asp Glu Cys
    1175   1180   1185

Leu Ser His Pro Cys Gln Asn Gly Gly Thr Cys Leu Asp Leu Pro
    1190   1195   1200

Asn Thr Tyr Lys Cys Ser Cys Pro Arg Gly Thr Gln Gly Val His
    1205   1210   1215

Cys Glu Ile Asn Val Asp Asp Cys Asn Pro Pro Val Asp Pro Val
    1220   1225   1230

Ser Arg Ser Pro Lys Cys Phe Asn Asn Gly Thr Cys Val Asp Gln
    1235   1240   1245

Val Gly Gly Tyr Ser Cys Thr Cys Pro Pro Gly Phe Val Gly Glu
    1250   1255   1260

Arg Cys Glu Gly Asp Val Asn Glu Cys Leu Ser Asn Pro Cys Asp
    1265   1270   1275

Ala Arg Gly Thr Gln Asn Cys Val Gln Arg Val Asn Asp Phe His
    1280   1285   1290

Cys Glu Cys Arg Ala Gly His Thr Gly Arg Arg Cys Glu Ser Val
    1295   1300   1305

Ile Asn Gly Cys Lys Gly Lys Pro Cys Lys Asn Gly Gly Thr Cys
    1310   1315   1320

Ala Val Ala Ser Asn Thr Ala Arg Gly Phe Ile Cys Lys Cys Pro
    1325   1330   1335

Ala Gly Phe Glu Gly Ala Thr Cys Glu Asn Asp Ala Arg Thr Cys
    1340   1345   1350

Gly Ser Leu Arg Cys Leu Asn Gly Gly Thr Cys Ile Ser Gly Pro
    1355   1360   1365

Arg Ser Pro Thr Cys Leu Cys Leu Gly Pro Phe Thr Gly Pro Glu
    1370   1375   1380

Cys Gln Phe Pro Ala Ser Ser Pro Cys Leu Gly Gly Asn Pro Cys
    1385   1390   1395

Tyr Asn Gln Gly Thr Cys Glu Pro Thr Ser Glu Ser Pro Phe Tyr
    1400   1405   1410

Arg Cys Leu Cys Pro Ala Lys Phe Asn Gly Leu Leu Cys His Ile
    1415   1420   1425

Leu Asp Tyr Ser Phe Gly Gly Gly Ala Gly Arg Asp Ile Pro Pro
    1430   1435   1440

Pro Leu Ile Glu Glu Ala Cys Glu Leu Pro Glu Cys Gln Glu Asp
    1445   1450   1455

Ala Gly Asn Lys Val Cys Ser Leu Gln Cys Asn Asn His Ala Cys
    1460   1465   1470

Gly Trp Asp Gly Gly Asp Cys Ser Leu Asn Phe Asn Asp Pro Trp
    1475   1480   1485

Lys Asn Cys Thr Gln Ser Leu Gln Cys Trp Lys Tyr Phe Ser Asp
    1490   1495   1500

Gly His Cys Asp Ser Gln Cys Asn Ser Ala Gly Cys Leu Phe Asp
    1505   1510   1515

Gly Phe Asp Cys Gln Arg Ala Glu Gly Gln Cys Asn Pro Leu Tyr
    1520   1525   1530

Asp Gln Tyr Cys Lys Asp His Phe Ser Asp Gly His Cys Asp Gln
    1535   1540   1545

Gly Cys Asn Ser Ala Glu Cys Glu Trp Asp Gly Leu Asp Cys Ala
    1550   1555   1560

Glu His Val Pro Glu Arg Leu Ala Ala Gly Thr Leu Val Val Val
    1565   1570   1575

Val Leu Met Pro Pro Glu Gln Leu Arg Asn Ser Ser Phe His Phe
    1580   1585   1590

Leu Arg Glu Leu Ser Arg Val Leu His Thr Asn Val Val Phe Lys
    1595   1600   1605

Arg Asp Ala His Gly Gln Gln Met Ile Phe Pro Tyr Tyr Gly Arg
    1610   1615   1620

Glu Glu Glu Leu Arg Lys His Pro Ile Lys Arg Ala Ala Glu Gly
    1625   1630   1635

Trp Ala Ala Pro Asp Ala Leu Leu Gly Gln Val Lys Ala Ser Leu
    1640   1645   1650

Leu Pro Gly Gly Ser Glu Gly Gly Arg Arg Arg Arg Glu Leu Asp
    1655   1660   1665

Pro Met Asp Val Arg Gly Ser Ile Val Tyr Leu Glu Ile Asp Asn
    1670   1675   1680

Arg Gln Cys Val Gln Ala Ser Ser Gln Cys Phe Gln Ser Ala Thr
    1685   1690   1695

Asp Val Ala Ala Phe Leu Gly Ala Leu Ala Ser Leu Gly Ser Leu
    1700   1705   1710

Asn Ile Pro Tyr Lys Ile Glu Ala Val Gln Ser Glu Thr Val Glu
    1715   1720   1725

Pro Pro Pro Pro Ala Gln Leu His Phe Met Tyr Val Ala Ala Ala
    1730   1735   1740

Ala Phe Val Leu Leu Phe Phe Val Gly Cys Gly Val Leu Leu Ser
    1745   1750   1755

Arg Lys Arg Arg Xaa Gln His Gly Gln Leu Trp Phe Pro Glu Gly
    1760   1765   1770

Phe Lys Val Ser Glu Ala Ser Lys Lys Lys Arg Arg Glu Xaa Leu
    1775   1780   1785

Gly Glu Asp Ser Val Gly Leu Lys Pro Leu Lys Asn Ala Ser Asp
    1790   1795   1800

Gly Ala Leu Met Asp Asp Asn Gln Asn Glu Trp Gly Asp Glu Asp
    1805   1810   1815

Leu Glu Thr Lys Lys Phe Arg Phe Glu Glu Pro Val Val Leu Pro
    1820   1825   1830

Asp Leu Asp Asp Gln Thr Asp His Arg Gln Trp Thr Gln Gln His
    1835   1840   1845

Leu Asp Ala Ala Asp Leu Arg Met Ser Ala Met Ala Pro Thr Pro
    1850   1855   1860

Pro Gln Gly Glu Val Asp Ala Asp Cys Met Asp Val Asn Val Arg
    1865   1870   1875

Gly Pro Asp Gly Phe Thr Pro Leu Met Ile Ala Ser Cys Ser Gly
    1880   1885   1890

```
Gly Gly  Leu Glu Thr Gly Asn  Ser Glu Glu Glu  Asp Ala Pro
    1895                1900              1905

Ala Val  Ile Ser Asp Phe Ile  Tyr Gln Gly Ala Ser  Leu His Asn
    1910                1915              1920

Gln Thr  Asp Arg Thr Gly Glu  Thr Ala Leu His Leu  Ala Ala Arg
    1925                1930              1935

Tyr Ser  Arg Ser Asp Ala Ala  Lys Arg Leu Leu Glu  Ala Ser Ala
    1940                1945              1950

Asp Ala  Asn Ile Gln Asp Asn  Met Gly Arg Thr Pro  Leu His Ala
    1955                1960              1965

Ala Val  Ser Ala Asp Ala Gln  Gly Val Phe Gln Ile  Leu Ile Arg
    1970                1975              1980

Asn Arg  Ala Thr Asp Leu Asp  Ala Arg Met His Asp  Gly Thr Thr
    1985                1990              1995

Pro Leu  Ile Leu Ala Ala Arg  Leu Ala Val Glu Gly  Met Leu Glu
    2000                2005              2010

Asp Leu  Ile Asn Ser His Ala  Asp Val Asn Ala Val  Asp Asp Leu
    2015                2020              2025

Gly Lys  Ser Ala Leu His Trp  Ala Ala Ala Val Asn  Asn Val Asp
    2030                2035              2040

Ala Ala  Val Val Leu Leu Lys  Asn Gly Ala Asn Lys  Asp Met Gln
    2045                2050              2055

Asn Asn  Arg Glu Glu Thr Pro  Leu Phe Leu Ala Ala  Arg Glu Gly
    2060                2065              2070

Ser Tyr  Glu Thr Ala Lys Val  Leu Leu Asp His Phe  Ala Asn Arg
    2075                2080              2085

Asp Ile  Thr Asp His Met Asp  Arg Leu Pro Arg Asp  Ile Ala Gln
    2090                2095              2100

Glu Arg  Met His His Asp Ile  Val Arg Leu Leu Asp  Glu Tyr Asn
    2105                2110              2115

Leu Val  Arg Ser Pro Gln Leu  His Gly Ala Pro Leu  Gly Gly Thr
    2120                2125              2130

Pro Thr  Leu Ser Pro Pro Leu  Cys Ser Pro Asn Gly  Tyr Leu Gly
```

```
        2135                    2140                    2145

Ser Leu  Lys Pro Gly Val Gln  Gly Lys Lys Val Arg  Lys Pro Ser
    2150                2155                2160

Ser Lys  Gly Leu Ala Cys Gly  Ser Lys Glu Ala Lys  Asp Leu Lys
    2165                2170                2175

Ala Arg  Arg Lys Lys Ser Gln  Asp Gly Lys Gly Cys  Leu Leu Asp
    2180                2185                2190

Ser Ser  Gly Met Leu Ser Pro  Val Asp Ser Leu Glu  Ser Pro His
    2195                2200                2205

Gly Tyr  Leu Ser Asp Val Ala  Ser Pro Pro Leu Leu  Pro Ser Pro
    2210                2215                2220

Phe Gln  Gln Ser Pro Ser Val  Pro Leu Asn His Leu  Pro Gly Met
    2225                2230                2235

Pro Asp  Thr His Leu Gly Ile  Gly His Leu Asn Val  Ala Ala Lys
    2240                2245                2250

Pro Glu  Met Ala Ala Leu Gly  Gly Gly Gly Arg Leu  Ala Phe Glu
    2255                2260                2265

Thr Gly  Pro Pro Arg Leu Ser  His Leu Pro Val Ala  Ser Gly Thr
    2270                2275                2280

Ser Thr  Val Leu Gly Ser Ser  Ser Gly Gly Ala Leu  Asn Phe Thr
    2285                2290                2295

Val Gly  Gly Ser Thr Ser Leu  Asn Gly Gln Cys Glu  Trp Leu Ser
    2300                2305                2310

Arg Leu  Gln Ser Gly Met Val  Pro Asn Gln Tyr Asn  Pro Leu Arg
    2315                2320                2325

Gly Ser  Val Ala Pro Gly Pro  Leu Ser Thr Gln Ala  Pro Ser Leu
    2330                2335                2340

Gln His  Gly Met Val Gly Pro  Leu His Ser Ser Leu  Ala Ala Ser
    2345                2350                2355

Ala Leu  Ser Gln Met Met Ser  Tyr Gln Gly Leu Pro  Ser Thr Arg
    2360                2365                2370

Leu Ala  Thr Gln Pro His Leu  Val Gln Thr Gln Gln  Val Gln Pro
    2375                2380                2385
```

Gln Asn Leu Gln Met Gln Gln Gln Asn Leu Gln Pro Ala Asn Ile
    2390   2395   2400

Gln Gln Gln Gln Ser Leu Gln Pro Pro Pro Pro Pro Pro Gln Pro
    2405   2410   2415

His Leu Gly Val Ser Ser Ala Ala Ser Gly His Leu Gly Arg Ser
    2420   2425   2430

Phe Leu Ser Gly Glu Pro Ser Gln Ala Asp Val
    2435   2440

<210> 7
<211> 30
<212> PRT
<213> Artificial sequence

<220>
<223> Amino acid sequence surrounding the transmembrane domains of APP

<400> 7

Ser Asn Lys Gly Ala Ile Ile Gly Leu Met Val Gly Gly Val Val Ile
1   5   10   15

Ala Thr Val Ile Val Ile Thr Leu Val Met Leu Lys Lys Lys
            20   25   30

<210> 8
<211> 30
<212> PRT
<213> Artificial sequence

<220>
<223> Sequence surrounding the transmembrane domains of E-cathedrin

<400> 8

Ile Pro Glu Trp Leu Ile Ile Leu Ala Ser Leu Leu Leu Ala Leu Ala
1   5   10   15

Leu Ile Leu Ala Val Cys Ile Ala Val Asn Ser Arg Arg Arg
            20   25   30

<210> 9
<211> 30
<212> PRT
<213> Artificial sequence

<220>
<223> Sequence surrounding the transmembrane domains of Notch-1

<400> 9

Pro Ser Gln Leu His Leu Met Tyr Val Ala Ala Ala Ala Phe Val Leu

```
Leu Phe Phe Val Gly Cys Gly Val Leu Leu Ser Arg Lys Arg
            20              25              30
```

<210> 10
<211> 158
<212> PRT
<213> Artificial sequence

<220>
<223> Sequence surrounding the transmembrane domains of Notch-1

<400> 10

```
Asn Ile Pro Tyr Lys Ile Glu Ala Val Lys Ser Glu Pro Val Glu Pro
1               5                   10                  15

Pro Leu Pro Ser Gln Leu His Leu Met Tyr Val Ala Ala Ala Ala Phe
            20              25              30

Val Leu Leu Phe Phe Val Gly Cys Gly Val Leu Leu Ser Arg Lys Arg
        35              40              45

Arg Arg Gln His Gly Gln Leu Trp Phe Pro Glu Gly Phe Lys Val Ser
    50              55              60

Glu Ala Ser Lys Lys Lys Arg Arg Glu Pro Leu Gly Glu Asp Ser Val
65              70              75              80

Gly Leu Lys Pro Leu Lys Asn Ala Ser Asp Gly Ala Leu Met Asp Asp
            85              90              95

Asn Gln Asn Glu Trp Gly Asp Glu Asp Leu Glu Thr Lys Lys Phe Arg
            100             105             110

Phe Glu Glu Pro Val Val Leu Pro Asp Leu Ser Asp Gln Thr Asp His
            115             120             125

Arg Gln Trp Thr Gln Gln His Leu Asp Ala Ala Asp Leu Arg Met Ser
    130             135             140

Ala Met Ala Pro Thr Pro Pro Gln Gly Glu Val Asp Ala Asp
145             150             155
```

<210> 11
<211> 8
<212> PRT
<213> Artificial sequence

<220>
<223> C-terminal flag sequence

<400> 11

Asp Tyr Lys Asp Asp Asp Asp Lys
1   5

<210> 12
<211> 16
<212> PRT
<213> Artificial sequence

<220>
<223> Flag/8 his tag

<400> 12

Asp Tyr Lys Asp Asp Asp Asp Lys His His His His His His His His
1   5   10   15

<210> 13
<211> 1665
<212> DNA
<213> Artificial sequence

<220>
<223> Nucleic acid encoding NusA

<400> 13

atgaacaaag aaattttggc tgtagttgaa gccgtatcca atgaaaaggc gctacctcgc   60

gagaagattt tcgaagcatt ggaaagcgcg ctggcgacag caacaaagaa aaaatatgaa   120

caagagatcg acgtccgcgt acagatcgat cgcaaaagcg gtgattttga cactttccgt   180

cgctggttag ttgttgatga agtcacccag ccgaccaagg aaatcaccct tgaagccgca   240

cgttatgaag atgaaagcct gaacctgggc gattacgttg aagatcagat tgagtctgtt   300

acctttgacc gtatcactac ccagacggca aaacaggtta tcgtgcagaa agtgcgtgaa   360

gccgaacgtg cgatggtggt tgatcagttc cgtgaacacg aaggtgaaat catcaccggc   420

gtggtgaaaa aagtaaaccg cgacaacatc tctctggatc tgggcaacaa cgctgaagcc   480

gtgatcctgc gcgaagatat gctgccgcgt gaaaacttcc gccctggcga ccgcgttcgt   540

ggcgtgctct attccgttcg cccggaagcg cgtggcgcgc aactgttcgt cactcgttcc   600

aagccggaaa tgctgatcga actgttccgt attgaagtgc agaaatcgg cgaagaagtg   660

attgaaatta aagcagcggc tcgcgatccg ggttctcgtg cgaaaatcgc ggtgaaaacc   720

aacgataaac gtatcgatcc ggtaggtgct tgcgtaggta tgcgtggcgc gcgtgttcag   780

gcggtgtcta ctgaactggg tggcgagcgt atcgatatcg tcctgtggga tgataacccg   840

gcgcagttcg tgattaacgc aatggcaccg gcagacgttg cttctatcgt ggtggatgaa   900

gataaacaca ccatggacat cgccgttgaa gccggtaatc tggcgcaggc gattggccgt   960

aacggtcaga acgtgcgtct ggcttcgcaa ctgagcggtt gggaactcaa cgtgatgacc   1020

gttgacgacc tgcaagctaa gcatcaggcg gaagcgcacg cagcgatcga caccttcacc   1080

```
aaatatctcg acatcgacga agacttcgcg actgttctgg tagaagaagg cttctcgacg      1140

ctggaagaat tggcctatgt gccgatgaaa gagctgttgg aaatcgaagg ccttgatgag      1200

ccgaccgttg aagcactgcg cgagcgtgct aaaaatgcac tggccaccat tgcacaggcc      1260

caggaagaaa gcctcggtga taacaaaccg gctgacgatc tgctgaacct tgaagggggta      1320

gatcgtgatt tggcattcaa actggccgcc cgtggcgttt gtacgctgga agatctcgcc      1380

gaacagggca ttgatgatct ggctgatatc gaagggttga ccgacgaaaa agccggagca      1440

ctgattatgg ctgcccgtaa tatttgctgg ttcggtgacg aagcgactag tggttctggt      1500

catcaccatc accatcactc cgcgggtaaa gaaaccgctg ctgcgaaatt tgaacgccag      1560

cacatggact cgccaccgcc aactggtctg gtcccccggg gcagcgcggg ttctggtacg      1620

attgatgacg acgacaagag tccgggagct cgtggatccg aattc                     1665
```

<210> 14
<211> 555
<212> PRT
<213> Artificial sequence

<220>
<223> Protein sequence encoding NusA

<400> 14

```
Met Asn Lys Glu Ile Leu Ala Val Val Glu Ala Val Ser Asn Glu Lys
1               5                   10                  15


Ala Leu Pro Arg Glu Lys Ile Phe Glu Ala Leu Glu Ser Ala Leu Ala
            20                  25                  30


Thr Ala Thr Lys Lys Lys Tyr Glu Gln Glu Ile Asp Val Arg Val Gln
        35                  40                  45


Ile Asp Arg Lys Ser Gly Asp Phe Asp Thr Phe Arg Arg Trp Leu Val
    50                  55                  60


Val Asp Glu Val Thr Gln Pro Thr Lys Glu Ile Thr Leu Glu Ala Ala
65                  70                  75                  80


Arg Tyr Glu Asp Glu Ser Leu Asn Leu Gly Asp Tyr Val Glu Asp Gln
                85                  90                  95


Ile Glu Ser Val Thr Phe Asp Arg Ile Thr Thr Gln Thr Ala Lys Gln
                100                 105                 110


Val Ile Val Gln Lys Val Arg Glu Ala Glu Arg Ala Met Val Val Asp
            115                 120                 125


Gln Phe Arg Glu His Glu Gly Glu Ile Ile Thr Gly Val Val Lys Lys
```

```
Val Asn Arg Asp Asn Ile Ser Leu Asp Leu Gly Asn Asn Ala Glu Ala
145             150             155             160

Val Ile Leu Arg Glu Asp Met Leu Pro Arg Glu Asn Phe Arg Pro Gly
             165             170             175

Asp Arg Val Arg Gly Val Leu Tyr Ser Val Arg Pro Glu Ala Arg Gly
             180             185             190

Ala Gln Leu Phe Val Thr Arg Ser Lys Pro Glu Met Leu Ile Glu Leu
             195             200             205

Phe Arg Ile Glu Val Pro Glu Ile Gly Glu Glu Val Ile Glu Ile Lys
             210             215             220

Ala Ala Ala Arg Asp Pro Gly Ser Arg Ala Lys Ile Ala Val Lys Thr
225             230             235             240

Asn Asp Lys Arg Ile Asp Pro Val Gly Ala Cys Val Gly Met Arg Gly
             245             250             255

Ala Arg Val Gln Ala Val Ser Thr Glu Leu Gly Gly Glu Arg Ile Asp
             260             265             270

Ile Val Leu Trp Asp Asp Asn Pro Ala Gln Phe Val Ile Asn Ala Met
             275             280             285

Ala Pro Ala Asp Val Ala Ser Ile Val Val Asp Glu Asp Lys His Thr
             290             295             300

Met Asp Ile Ala Val Glu Ala Gly Asn Leu Ala Gln Ala Ile Gly Arg
305             310             315             320

Asn Gly Gln Asn Val Arg Leu Ala Ser Gln Leu Ser Gly Trp Glu Leu
             325             330             335

Asn Val Met Thr Val Asp Asp Leu Gln Ala Lys His Gln Ala Glu Ala
             340             345             350

His Ala Ala Ile Asp Thr Phe Thr Lys Tyr Leu Asp Ile Asp Glu Asp
             355             360             365

Phe Ala Thr Val Leu Val Glu Glu Gly Phe Ser Thr Leu Glu Glu Leu
             370             375             380

Ala Tyr Val Pro Met Lys Glu Leu Leu Glu Ile Glu Gly Leu Asp Glu
385             390             395             400
```

```
Pro Thr Val Glu Ala Leu Arg Glu Arg Ala Lys Asn Ala Leu Ala Thr
             405                 410              415

Ile Ala Gln Ala Gln Glu Glu Ser Leu Gly Asp Asn Lys Pro Ala Asp
             420                 425              430

Asp Leu Leu Asn Leu Glu Gly Val Asp Arg Asp Leu Ala Phe Lys Leu
             435                 440              445

Ala Ala Arg Gly Val Cys Thr Leu Glu Asp Leu Ala Glu Gln Gly Ile
    450                 455                 460

Asp Asp Leu Ala Asp Ile Glu Gly Leu Thr Asp Glu Lys Ala Gly Ala
465                 470                 475                 480

Leu Ile Met Ala Ala Arg Asn Ile Cys Trp Phe Gly Asp Glu Ala Thr
             485                 490              495

Ser Gly Ser Gly His His His His His His Ser Ala Gly Lys Glu Thr
             500             505                 510

Ala Ala Ala Lys Phe Glu Arg Gln His Met Asp Ser Pro Pro Pro Thr
             515             520                 525

Gly Leu Val Pro Arg Gly Ser Ala Gly Ser Gly Thr Ile Asp Asp Asp
    530             535                 540

Asp Lys Ser Pro Gly Ala Arg Gly Ser Glu Phe
545             550                 555
```